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*"Education, health, and literacy are particularly crucial to the completion of the fertility transition."*

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Volume 8, Number 1

### EPIDEMIOLOGY

## *What Factors Affect the Prevalence of HIV in sub-Saharan Africa?*

More than 3 million of the 5 million people who were newly infected with HIV in 2001 live in sub-Saharan Africa, according to UNAIDS. The vast majority of HIV-infected adults in Africa acquired their infection through heterosexual intercourse. Over the decades since the AIDS epidemic was first noted, researchers have observed that the prevalence of HIV infection within Africa varies greatly. While many areas in East and Southern Africa experience high rates of infection, regions in West and Central Africa generally have lower infection rates. A number of theories to explain these disparities have been put forth. But until now there have been no systematic studies to directly address this matter.

Two Population Council researchers, Jane Chege, then based in Nairobi, Kenya, and Naomi Rutenberg, based in Washington, DC, participated along with several other investigators in a recent study on HIV. Chege is now based in Johannesburg, South Africa. The findings of the investigation, known as the multicentre study of factors determining the different prevalences of HIV in sub-Saharan Africa, were presented in a special supplement to the journal *AIDS*. The Population Council collaborated on the study design and questionnaires and collected data in one location, Kisumu, Kenya. Chege and Rutenberg assessed data quality and analyzed data at the population and individual level. This analysis suggested further avenues of investigation, which were pursued by the other scientists. The research findings indicate that changes in HIV-prevention policy are urgently needed.

The researchers investigated HIV epidemics in four cities. Two of these cities—Kisumu and Ndola, Zambia, in East and Southern Africa—have a high HIV prevalence. And two—Cotonou, Benin and Yaoundé, Cameroon, in West and Central Africa—have a low and stable HIV prevalence. In each of these cities, researchers selected approximately 1,000 men and 1,000 women aged 15–49 years from the general population. Those who agreed to participate were interviewed about sexual behaviors and other factors that might influence their susceptibility to HIV infection. They were tested for HIV and a number of other sexually transmitted infections (STIs).

### *HIV prevalence in young women*

The HIV testing conducted as part of the study confirmed a high HIV prevalence in Kisumu and Ndola. It also underlined the greater risk of infection experienced by women, particularly young women, compared to men.

A group of researchers, including Chege, analyzed the statistics from Kisumu and Ndola. They found that among sexually active 15–19-year-olds in both sites, HIV was six times more prevalent in women than in men. Among 20–24-year-olds, the infection was three times more prevalent in women. HIV was equally widespread among women and men in the 25–49 year age group.

Behavioral factors did not seem to explain this difference in HIV susceptibility. The presence of

*continued on page 8*

# Public Services Found Lacking in Many Developing-Country Cities

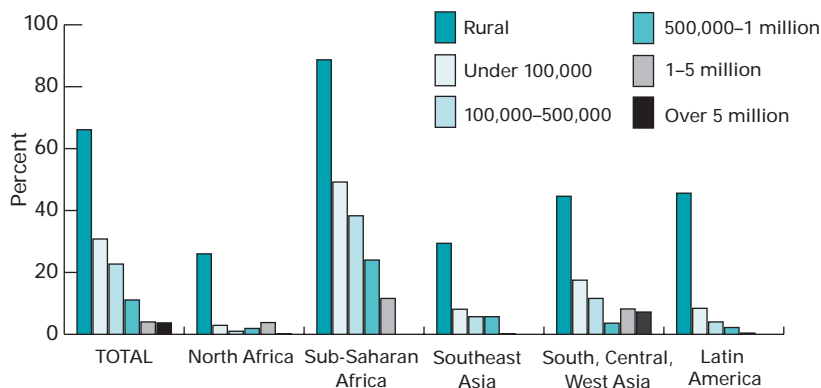
In the cities of less-developed countries, many households are not outfitted with running water, sanitary waste disposal, and electricity. Poor water quality and inadequate sanitation are associated with increased incidence of diarrheal diseases, such as cholera, and other bacterial pathogens. Furthermore, these diseases can recur and affect health in the long term by reducing the uptake of nutrients, which in turn stunts growth and causes wasting. Children living without these basic public services also suffer from elevated mortality and other health risks. Lack of electricity can influence nutrition directly, by limiting refrigeration and food storage, and indirectly, by reducing economic production and incomes.

Population Council demographers Paul C. Hewett and Mark R. Montgomery recently completed a comprehensive examination of the availability of services in cities and towns of developing countries around the world. Using data from the Demographic and Health Surveys of 43 countries, they discovered striking differences in the distribution of these basic services. Moreover, recent political changes underway in many developing countries may be making the delivery of basic services more difficult.

## Smaller cities and the urban poor

Research has often detailed the extreme deprivation in rural areas of developing countries. In rural sub-Saharan Africa, for instance, nearly 90 percent of households (representing more than 350 million people) lack running water, flush toilets, and electricity. However, "in addition to highlighting the needs of the rural poor," says Hewett, "our research suggests that the circumstances of the urban poor, particularly those in smaller cities, require attention." The United Nations projects that in the next quarter-century, more than 90 percent of world population growth will occur in urban areas of developing countries.

Percent of households lacking piped water, flush toilet, and electricity by city size



By distinguishing urban areas by size rather than merely focusing on differences between urban and rural areas or on the largest cities, Hewett and Montgomery found that people who live in smaller cities are much less likely to have basic services than are people who live in larger cities. For instance, nearly 50 percent of households in the cities of sub-Saharan Africa with populations under 100,000 lack piped water, flush toilets, and electricity. Similar deficits in the availability of basic services exist in the smaller cities of Asia and Latin America.

"We also found sharp inequalities in access to public services between the urban poor and other urban residents," says Hewett. The largest differences emerge in access to electricity, which in sub-Saharan African countries is available to only a quarter of the urban poor but slightly more than half of other urban households. Wide differentials in access are also evident in Southeast Asia, and in South, Central, and West Asia. In Latin America, the greatest differences between the urban poor and other urban residents are seen in access to flush toilets, with smaller (yet still significant) differences in piped water and electricity.

## Political decentralization and devolution

Recent policy changes may stymie efforts to remedy these imbalances. "Many developing-country governments are decentralizing service delivery, transferring responsibilities from national to local levels without a commensurate transfer of funding," says Montgomery. "This leaves local governments unable to extend public services." In some cases non-governmental organizations, community-based organizations, and residents' associations have attempted to provide services. The researchers contend, however, that such small groups may not effectively substitute for active national governments. "Until the situation is sorted out, gross inefficiencies and gaps will probably continue to plague the provision of public services," contends Montgomery. ■

### SOURCE

Hewett, Paul C. and Mark R. Montgomery. 2001. "Poverty and public services in developing-country cities." Policy Research Division Working Paper no. 154. New York: Population Council.

### OUTSIDE FUNDING

The William and Flora Hewlett Foundation, The Andrew W. Mellon Foundation, and the United States Agency for International Development

# *Decelerating Pace and Human Development Crucial Elements of Fertility Transition*

In a small number of developing countries fertility has dipped below the replacement level of 2.1 births per woman. Some demographers have asked whether projections of future population growth might be made more accurate by changing them to assume that fertility in the long run will fall below replacement in all countries, rather than to 2.1 births per woman as is now the assumption. If fertility declines to 2.1 births per woman, population will peak in the twenty-second century and then stabilize. If fertility declines to 1.8 or 1.9 births per woman, on the other hand, population will peak late in this century and then begin a slow decline.

In March 2002, a United Nations expert group met to debate the possibility of revising the UN methodology for projecting the course of population growth over the next several decades. Population Council demographer John Bongaarts, one of the experts called to comment on this issue, contends that simply lowering the assumed ultimate fertility level would be insufficient. He recently published research outlining additional changes that would be needed to make the fertility projection model more accurate.

"The UN has been tremendously successful at predicting population growth in the past, but a close look at their projections suggests several ways to improve them," says Bongaarts. A slight reduction in the assumed fertility level at the end of the transition to about 1.9 is a step in the right direction. "Other adjustments are also desirable, although once the necessary adjustments are made, population projections into the middle of this century will still be similar to the current UN projections."

## *Pace of fertility transition*

The current UN model for future fertility decline does not take into account the changing pace of fertility. The model assumes a linear drop to a stable fertility level of 2.1 births per woman in most developing countries. The

research of Bongaarts and other Population Council investigators shows, however, that the speed of fertility decline changes as the transition from high to low fertility progresses.

In his recent study, Bongaarts examined trends and patterns in fertility in the developing world, focusing particularly on the later stages of transition. He sought to identify regularities in the past record that may provide

*"Poor countries with high levels of health and education can have low fertility."*

clues to future trends. Bongaarts looked at UN estimates of total fertility rates between the years 1950 and 2000 for all countries of Africa, Asia, and Latin America and the Caribbean except Japan, Australia, and New Zealand. Past fertility trends have been highly variable. Some countries—Singapore and South Korea, for example—proceeded fairly swiftly to below-replacement-level fertility. Others, mostly in sub-Saharan Africa, still have high fertility. Rapid declines to below replacement are the exception rather than the rule.

Three key features summarize these past transitions. First, fertility is high until the transition begins. Second, once the transition gets underway, fertility declines fairly rapidly. And third, the pace of decline decelerates as countries reach the later stages of the transition. Sometimes the fertility transition stalls above replacement level for decades. These same patterns are likely to prevail in the future, and they should be incorporated in projections. In the future many developing countries will experience slower declines than the UN now assumes.

Bongaarts also looked at several indicators of development to see whether these had any bearing on the fertility transition. Some observers have argued that, despite conventional wisdom, development may play little role in reducing fertility. "The beginning of the fertility transition is often driven by the diffusion of new ideas about reproductive behavior among individuals, communities, and countries," says Bongaarts. "Education, health, and literacy, however, are particularly crucial to the completion of the fertility transition. Wealth is less critical. Poor countries, such as Sri Lanka, with high levels of health and education can have low fertility." Bongaarts's investigation revealed that most developing countries that have attained near-replacement fertility levels have an average life expectancy of more than 70 years and a literacy level over 90 percent. The large majority of developing countries fall well short of this level of human development. Thus, considerable progress will likely have to be made before near-replacement fertility becomes widespread, Bongaarts contends.

One reason that reaching replacement-level fertility is difficult is that it requires a high degree of birth control. Diligent, effective use of family planning is needed to avoid unintended pregnancies. "A high-quality family planning program can move a country closer to replacement fertility than would be expected from its level of development alone," explains Bongaarts. "But these programs alone cannot bring about declines in desired family size. Human development is the key to reducing preferences for large families and to completing the transition." ■

## SOURCE

Bongaarts, John. 2002. "The end of the fertility transition in the developing world." Policy Research Division Working Paper no. 161. New York: Population Council.

## OUTSIDE FUNDING

The William and Flora Hewlett Foundation, The Andrew W. Mellon Foundation, and the United States Agency for International Development



# *Illuminating the Role of Inhibins and Activins in Fertility*

All currently available hormonal contraceptives for women reduce fertility by influencing levels of the steroid hormones estrogen and progesterone. Altering the levels of these hormones, however, can cause unpleasant side effects in some cases. Population Council molecular endocrinologist Daniel Bernard is conducting basic research that may one day lead to a contraceptive for women that leaves estrogen and progesterone levels largely unaffected, theoretically resulting in fewer side effects. His research concerns two types of protein hormones that play a role in women's fertility: inhibins and activins.

## *Interplay of hormones*

Successful reproduction is dependent upon the coordinated regulation and actions of hormones created in the brain, the pituitary gland, and the ovary and testis. In women, for example, various hormones stimulate the maturation of egg-containing follicles in the ovaries. They also trigger ovulation and prepare the uterus for the implantation of fertilized eggs. Feedback loops, in which levels of one hormone influence the production of other hormones, control this monthly cycle.

One vital hormone involved in female fertility is follicle-stimulating hormone (FSH). The anterior pituitary gland releases FSH, which then travels to the ovary via the bloodstream. In the ovary, FSH binds to molecular receptors on the surface of cells. The binding of a protein or hormone to a receptor can be thought of as a key entering a lock. When the FSH "key" binds with its receptor "lock," it stimulates the growth of follicles.

Women who cannot produce FSH or its molecular receptors are infertile because their egg-containing follicles are unable to mature. Drugs that block the action of FSH would be likely to produce reversible infertility in women. (FSH does not appear to be necessary for reproduction in men.)

Many hormones regulate the production of FSH. Bernard, however, is most interested in

pursuing inhibins, which are produced in the ovary and testis, and activins, which appear to affect FSH through their local production within the pituitary gland. As their names suggest, inhibins hinder and activins stimulate the production and release of FSH from the pituitary. Moreover, these hormones selectively influence FSH production and do not directly affect either estrogen or progesterone production.

*"Learning how inhibins and activins regulate FSH is critical to understanding the processes governing normal reproduction."*

Investigation into inhibins may also shed light on some diseases. Research has shown that abnormal inhibin production may contribute to the halt in follicle development seen in polycystic ovary syndrome, a disease that can cause infertility and other complications. And women with a rare form of ovarian cancer frequently have abnormal blood levels of inhibin. Both inhibin and activin are part of a larger family of proteins that seem to act as tumor suppressors.

## *Gaps in knowledge*

While much has been learned about how activins affect their target cells, there are still gaps in knowledge. Bernard and his colleagues aim to elucidate the cascade of actions generated within cells after the activin "key" binds to one of its "locks," a receptor known as ActRII. This sequence prompts the production of FSH.

The lab also seeks to clarify the mechanisms of action used by inhibins. One way that

inhibin hampers the production of FSH is by binding to ActRII, thus blocking activin from binding. Research has shown that alone, inhibin binds only weakly to ActRII. When certain other proteins are present, however, inhibin can bind strongly to the receptor.

One of these proteins is known as betaglycan. When inhibins interact with betaglycan and bind to ActRII receptors, they do not appear to set off a cascade of signals within the cell. Rather, they seem to work simply by disrupting activin action. As when the wrong key is put in a lock, the lock will not open and the inserted key prevents the correct key from entering.

Bernard and his team are investigating the possibility that inhibin–receptor binding sets off an unknown process within cells. They are also searching for proteins in the pituitary gland that are similar to betaglycan and for receptors that may be specific to inhibin—in other words a lock that inhibin can open.

Recently, Bernard and his colleagues discovered and began to characterize a protein, which they named InhBP/p120, that seems to exert some influence over inhibin activity. They showed that InhBP/p120 can form a complex with a different activin receptor, this one called ALK4. When inhibins are added, activin-stimulated gene activity stops almost entirely.

"Learning how inhibins and activins regulate FSH is critical to understanding the processes governing normal reproduction," says Bernard. "Understanding these processes may reveal targets for contraceptives, and may also give us insights into some forms of infertility and certain cancers, as well." ■

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## Bridging the Safe Motherhood Knowledge Gap

A reduction in maternal deaths, the goal of safe motherhood programs over the last decade and a half, has proved elusive. This may be due in part to the fact that safe motherhood programs often have been created on the basis of ideas that initially seemed good but had not been demonstrated to be effective. Two recent studies led by Council researchers have highlighted the need for identifying effective approaches before implementing them on a large scale.

### Self-reporting of symptoms

Ninety-nine percent of maternal deaths occur in developing countries, where fewer than 50 percent of women give birth in health facilities. In these resource-poor settings, life-threatening obstetric conditions often go unidentified. Women do not know when they require special obstetric care, and in rural areas where health services are scarce, pregnancy complications are frequently not properly managed.

Attempts to use risk factors to predict which women are likely to experience serious complications have been unsuccessful. Researchers had hoped that women's self-reports of symptoms could be used as a means to indicate life-threatening complications requiring referral and management.

In conjunction with the Kintampo Health Research Centre, Ghana, Council researchers conducted a retrospective study to determine whether it was possible to use women's self-reported obstetric symptoms to identify pregnancy complications. The investigators interviewed and assessed 340 consenting women who presented themselves to the Holy Family Hospital from the seventh month of pregnancy to 42 days postpartum.

Researchers used clinical examination and laboratory testing to determine women's health status. Self-reported symptoms were then compared with clinical findings of obstetric complications. Sixty-seven women (20 percent) experienced one or more complications. Complex algorithms correctly identified the majority of complicated and

uncomplicated pregnancies. These tools, however, missed 24 percent of cases requiring emergency obstetric care and incorrectly identified 25 percent of uncomplicated cases as requiring special obstetric management. Simple individual questions that could be used at the community level did not predict obstetric complications.

These findings are consistent with results from studies conducted in rural settings in other developing countries. Together, these studies show that the symptoms that best identified each obstetric condition varied across cultures. Therefore, algorithms to identify which women require referral would need to be developed and tested individually for each location. Given current knowledge and diagnostics, health programs are unlikely to develop successful systems to identify and refer women for obstetric management in areas with limited health care services.

### Causes of maternal death

In developing countries where medical services are scarce, many women deliver at home. In general, understanding of the medical and social causes of maternal death is incomplete because it is based on reports, called "verbal autopsies," of relatives and neighbors who have no medical training. In Mexico, the Council conducted a large "verbal autopsy" study to identify the causes of maternal death and disease. Data pertaining to 145 maternal deaths that occurred in 1995 in the states of Guerrero, Querétaro, and San Luis Potosí were reanalyzed.

Using the same data, but comparing different systems of classification, the researchers' calculations showed large variations in the attributed causes of women's deaths. The analyses, for example, demonstrated that postpartum hemorrhage might play a role in anywhere between 14 percent and 52 percent of maternal deaths.

In addition to demonstrating the inherent limitations of the verbal autopsy methodology,

the study also reconfirmed that mortality among poor women with little access to medical care is substantially higher than that among wealthier women who have better access to institutional delivery and postpartum care.

"This study suggests that although we know, in principle, the major medical causes of maternal death, we do not know the relative contribution of these various causes," says Population Council program associate Nancy L. Sloan, lead author of the article. However, she contends, program managers may not always need this knowledge to save women's lives. Over half of the 145 maternal deaths were associated with more than one complication. But preventing or managing any one of these conditions—postpartum hemorrhage, for example—could potentially save lives by reducing the gravity of the other obstetric conditions women experience.

"While we must continue our efforts to ensure adequate emergency obstetric care for all," says Beverly Winikoff, director of the Council's reproductive health program, "there may be ways to prevent life-threatening obstetric conditions that could feasibly and significantly reduce deaths." Population Council researchers are currently conducting a study of a strategy for reducing the incidence and severity of postpartum hemorrhage among women having home births in rural areas. ■

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### OUTSIDE FUNDING

Canadian International Development Agency, UNICEF, and The World Bank

## Motivations for and Barriers to Study Participation

What factors motivate people to participate in clinical trials? While participants may potentially reap benefits, the products being tested are, by definition, unproven. To gain insight into this question—particularly in reference to trials of microbicides—Population Council researchers, with colleagues at the Thailand Ministry of Public Health–U.S. Centers for Disease Control and Prevention Collaboration, recently assessed the interests and concerns of women in Chiang Rai, Thailand regarding participation in microbicide clinical trials. Findings from this and similar research may prove valuable for selecting trial sites, estimating enrollment rates, and tailoring trials to best meet women's needs.

Microbicides are products, such as gels, creams, or other formulations, designed to prevent sexually transmitted infections, including HIV, when applied vaginally or rectally before intercourse. While no microbicides are currently approved, a number of them—including one developed by the Council, known as Carraguard™—are being tested.

### Representative population

Many effectiveness trials of candidate microbicides have been conducted among sex workers. This practice, however, is not ideal. "Sex workers may have mucosal irritation from frequent intercourse," says Population Council researcher Charlotte Ellertson, "which might negate benefits of an otherwise effective microbicide." Many researchers would prefer to test microbicides among women who are more representative of the general population.

Investigators chose to study women in Chiang Rai, the northernmost province of Thailand, because the region has a high rate of HIV infection. They used a structured questionnaire to interview 370 women recruited from an antenatal and a family planning clinic. The survey questions were developed on the basis of findings from a series of focus group discussions and in-depth interviews of women and men in the province; only women participated

in the interviews. Before being interviewed, the women attended a brief informational session on microbicides and the requirements of a hypothetical clinical trial.

Eleven of the survey questions tested comprehension of information presented on microbicides and clinical trials. Eighty-two percent of the women answered eight or more of these questions correctly, while only 10 percent answered five or more questions incorrectly.

*"Doing something good for women's health" was the most important motivation in deciding to join a trial.*

After the short informational session, women were able to understand the most important concepts about microbicides and participation in clinical trials.

### Motivations and barriers

The researchers asked the participants to rank each of 13 motivations for trial participation as "most important," "very important," "somewhat important," or "not at all important." Eighty-two percent said that "getting tested for HIV during trial participation" was very important, whereas only 34 percent thought that getting reimbursed for travel costs was very important. Nearly half the women, however, thought this factor was somewhat important. When asked which motivation was the single most important in deciding to join a trial, "doing something good for women's health" was most often (35 percent) cited.

The researchers also asked participants to rank each of 19 barriers to trial participation as

"most important," "a major problem," "a small problem," or "not a problem." Forty-six percent of participants said that the fear that using a microbicide might cause their husband to feel protected and thus to have more sexual partners was a major problem. Forty-two percent of women thought that "deciding to participate in the trial without your husband's consent" was a major problem. More than 60 percent of women, however, stated that the need for regular follow-up was not a problem, and 67 percent said that fear of receiving HIV results was not a problem. When asked to name the single most important barrier to trial participation, women most often (27 percent) cited the fact that long-term side effects of a microbicide are not known.

Most women (two-thirds) said they thought they would be willing to participate in a trial, but wanted to consider the matter further. Roughly 6 percent asserted they were definitely willing to participate in a trial, and less than 3 percent said they were not at all willing to participate.

Noting that a similar study conducted in Bangkok regarding vaccine trials found a much higher proportion of people (51 percent) definitely willing to participate in trials, Council researcher Kelly Blanchard stated that "some uncertainty about trial participation may come from a lack of familiarity with microbicides as a concept. Information for potential trial participants and good counseling might mean more women would be willing to participate." Given that the two factors most frequently cited as a major problem involve women's husbands, the researchers concluded that outreach and education for men about microbicides would also be useful. ■

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other STIs, especially ones that result in ulcerated lesions, may account for some increased transmission of HIV. In both cities, for example, the rate of infection with herpes simplex virus type 2 was roughly four times greater among young women than among young men. Even when no other STI was present, however, young women were still at higher risk for HIV infection. There is evidence of high rates of HIV positivity following only a few episodes of sexual intercourse, suggesting that young women have a high susceptibility to infection.

## Male circumcision

The exposure of mucosal surfaces to HIV-containing secretions may account for another discrepancy in HIV prevalence seen in sub-Saharan Africa. A growing body of research shows that uncircumcised men in sub-Saharan Africa are about twice as likely as circumcised men to be infected with HIV. The foreskin of the penis, which is removed during circumcision, is lined with a mucous membrane. The prevalence of male circumcision varies across the continent. In Yaoundé and Cotonou nearly all men studied were circumcised. In Kisumu, roughly 28 percent of men studied were circumcised and in Ndola the figure was only 9 percent.

The researchers found three HIV risk factors that were more prevalent in Kisumu and Ndola than in Cotonou and Yaoundé: being married or having been married (among women and men), lack of circumcision (among men), and increased infection with herpes simplex virus type 2 (among women). The HIV risk associated with marriage may reflect the exposure of men and women, through repeated sexual intercourse, to spouses infected with HIV.

The investigators found a strong protective effect of male circumcision in Kisumu. The prevalence of HIV, herpes simplex virus type 2, and syphilis was significantly lower in circumcised men there.

The researchers conclude that the evidence of circumcision's protective effect against HIV is convincing and that the provision of safe male circumcision should be considered as part of the public health strategy to reduce the spread

of HIV. "But more research is needed to determine acceptability, feasibility, and cost-effectiveness," assert the investigators. Moreover, interventions to introduce circumcision must be carefully evaluated as they proceed.

The Population Council's Horizons program recently developed a research agenda on male circumcision that should contribute to feasibility studies. USAID-funded Horizons research is conducted in collaboration with the International Center for Research on Women, the Program for Appropriate Technology in Health, the International HIV/AIDS Alliance, Tulane University, Family Health International, and Johns Hopkins University.

## Key implications

In addition to highlighting the urgent need for more research and policy development regarding male circumcision, the study's findings suggest other key changes, say the researchers. "Infection with herpes simplex virus type 2 and HIV are extremely prevalent in young women shortly after they begin sexual activity," says Chege.

"Policymakers should strengthen community and school-based peer education for young women and men before they start sexual activity."

Additionally, "because HIV is likely to be transmitted between spouses, voluntary HIV counseling and testing among couples, particularly before marriage, should be encouraged," says Rutenberg. The researchers also called for community-based education to help people recognize the symptoms of herpes simplex virus type 2. During outbreaks, people infected with this virus can temporarily abstain from sex or use condoms in order to reduce transmission. ■

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